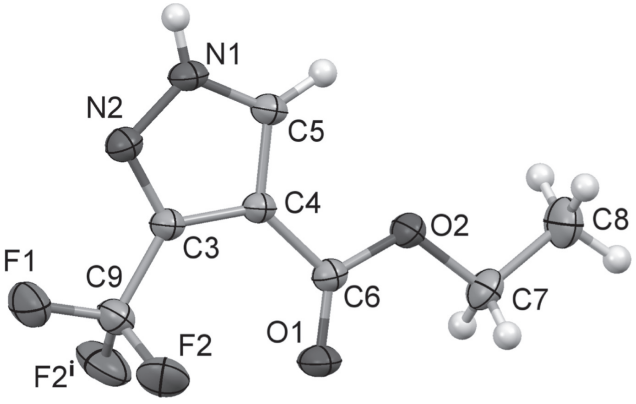
Željko. K. Jaćimović*, Sladjana B. Novaković, Goran A. Bogdanović, Milica Kosović, Eugen Libowitzky and Gerald Giester

Crystal structure of ethyl 3-(trifluoromethyl)-1*H*-pyrazole-4-carboxylate, $C_7H_7F_3N_2O_2$



https://doi.org/10.1515/ncrs-2020-0242
Received May 19, 2020; accepted June 2, 2020; available online June 20, 2020

Abstract

$C_7H_7F_3N_2O_2$, monoclinic, $P2_1/m$ (no. 11), $a = 6.8088(8)$ Å, $b = 6.7699(9)$ Å, $c = 9.9351(12)$ Å, $\beta = 105.416(3)°$, $V = 441.48(9)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0398$, $wR_{ref}(F^2) = 0.1192$, $T = 200(2)$ K.

CCDC no.: 2007110

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

***Corresponding author: Željko. K. Jaćimović,** Faculty of Metallurgy and Technology, Džordža Vašingtona bb, University of Montenegro, Podgorica, Montenegro, e-mail: zeljkoj@ucg.ac.me. https://orcid.org/0000-0001-6803-3835
Sladjana B. Novaković and Goran A. Bogdanović: Department of Theoretical Physics and Condensed Matter Physics, „VINČA“ Institute of Nuclear Sciences – National Institute of the Republic of Serbia, University of Belgrade, Belgrade, Serbia
Milica Kosović: Faculty of Metallurgy and Technology, Džordža Vašingtona bb, University of Montenegro, Podgorica, Montenegro
Eugen Libowitzky and Gerald Giester: Institut für Mineralogie und Kristallographie, Althanstra&se 14, Universität Wien – Geozentrum, Wien, Austria

Table 1: Data collection and handling.

Crystal:	Colorless prism
Size:	0.32 × 0.19 × 0.08 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.16 mm^{-1}
Diffractometer, scan mode:	Bruker Apex-II, φ and ω
θ_{max}, completeness:	33.2°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	17052, 1819, 0.025
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1466
$N(param)_{refined}$:	86
Programs:	Bruker [1], SHELX [2, 3], Platon [4], Mercury [5]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	x	y	z	U_{iso}*/U_{eq}
F1	0.43896(17)	0.2500	0.08691(10)	0.0588(4)
F2	0.67754(12)	0.40673(15)	0.23115(9)	0.0573(3)
O1	0.85926(15)	0.2500	0.52269(12)	0.0416(3)
O2	0.70241(15)	0.2500	0.69374(10)	0.0336(2)
N1	0.16706(17)	0.2500	0.39173(13)	0.0314(3)
N2	0.23079(17)	0.2500	0.27439(13)	0.0319(3)
C3	0.43220(19)	0.2500	0.32107(13)	0.0263(2)
C4	0.49813(18)	0.2500	0.46784(13)	0.0235(2)
C5	0.31902(19)	0.2500	0.50850(14)	0.0272(3)
H5	0.3066	0.2500	0.6015	0.033*
C6	0.70491(19)	0.2500	0.56073(14)	0.0265(3)
C7	0.8989(2)	0.2500	0.79805(16)	0.0369(3)
H7A	0.9783	0.3688	0.7875	0.044*
C8	0.8546(3)	0.2500	0.93749(18)	0.0520(5)
H8A	0.9829	0.2500	1.0112	0.078*
H8B	0.7758	0.1318	0.9463	0.078*
C9	0.5551(2)	0.2500	0.21712(15)	0.0363(3)
H1N	0.041(3)	0.2500	0.387(2)	0.042(5)*

Source of material

The 4 cm^3 of warm ethanolic solution of ethyl 3-(trifluoromethyl)-1*H*-pyrazole-4-carboxylate (Sigma-Aldrich) and 3 cm^3 of warm ethanolic solution of $Zn(OAc)_2 \cdot 2H_2O$ was mixed in ratio 1:2. The resulting unicolor solution was allowed to concentrate at ambient conditions for 3 days and the investigated sample material was filtered

off and washed with ethanol. Colorless crystals of ethyl 3-(trifluoromethyl)-1*H*-pyrazole-4-carboxylate were obtained.

Experimental details

H atoms bonded to C atoms were placed at geometrically idealized positions and refined as riding atoms [C—H = 0.95–0.99 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ or $1.5U_{eq}(C)$]. H atom attached to N atom was located in difference Fourier maps and refined isotropically.

Comment

Pyrazole derived compounds possess a wide range of biological activities including antimicrobial, antiviral, anti-inflammatory, anticancer, analgesic, antipyretic [6–8]; accordingly, the pyrazole fragment represents an important component of a number of therapeutic drugs [8 and references therein]. The presence of fluoroalkyl substituents on the pyrazole ring, as is the case with the pyrazole based drug Celebrex, can improve the lipophilicity and solubility of a molecule and thus influence its biological activity [9]. Also, the incorporation of carboxylic acid groups and carboxylic ester functionality facilitates further modification and improvement of bioactivity of the pyrazole based molecules [10]. As a part of our continuous research interest in the pyrazole derived compounds [11–13] we report here the crystal structure of ethyl 3-(trifluoromethyl)-1*H*-pyrazole-4-carboxylate.

In the title pyrazole derivative the pyrazole ring attaches the fluoroalkyl and carboxylic ester substituents. The molecule lies on a crystallographic mirror plane thus the constituent atoms are coplanar, with the exception of F and H atoms attached to sp^3 carbon atoms (see the figure). Bond lengths and angles are in the expected ranges [13–15]. In the crystal the molecules interact by N1—H1···O1^{ii} hydrogen bonds [H···O 2.06(3) Å; N—H···O 137(2)°; symmetry code: (ii) $x - 1, y, z$] to form a chain along the crystallographic *a* axis. The pyrazole hydrogen bonding acceptor N2 involves only in a long contact with the terminal ester carbon, C8—H8a···N2^{ii} [H···N 2.71 Å; C—H···O 158°; symmetry code: (iii) $x+1, +y, +z+1$]. The planar molecules form the layered structure parallel to (010) plane. The mutual distance between the neighboring layers is 3.385 Å [symmetry code (i) $= x, -y+1/2, z$].

Acknowledgements: M. K. and Ž.K.J. thank to the Ministry of Science of the Republic of Montenegro for financial support (Innovative Project-Bioextra); G.A.B and S.B.N thank to the Ministry of Education, Science and Technological Development of the Republic of Serbia for financial support.

References

1. Bruker. APEXII, SAINT-Plus, SADABS. Bruker AXS Inc., Madison, WI, USA (2008).
2. Sheldrick, G. M.: SHELXT – Integrated space-group and crystal-structure determination. Acta Crystallogr. **A71** (2015) 3–8.
3. Sheldrick, G. M.: Crystal structure refinement with SHELXL. Acta Crystallogr. **C71** (2015) 3–8.
4. Spek, A. L.: Single-crystal structure validation with the program PLATON. J. Appl. Crystallogr. **36** (2003) 7–13
5. Macrae, C. F.; Sovago, I.; Cottrell, S. J.; Galek, P. T. A.; McCabe, P.; Pidcock, E.; Platings, M.; Shields, G. P.; Stevens, J. S.; Towler, M.; Wood, P. A.: Mercury 4.0: from visualization to analysis, design and prediction. J. Appl. Crystallogr. **53** (2020) 226–235.
6. Faraz Khan, M.; Mumtaz Alam, M.; Verma, G.; Akhtar, W.; Akhter, M.; Shaquiquzzaman, M.: The therapeutic voyage of pyrazole and its analogs: a review. Eur. J. Med. Chem. **120** (2016) 170–201.
7. Alam, J.; Alam, O.; Alam, P.; Naim, M. J.: A review on pyrazole chemical entity and biological activity. Int. J. Pharm. Sci. Res. **6** (2015) 1433–1442.
8. Naim, M. J.; Alam, O.; Nawaz, F.; Alam, J.; Alam, P.: Current status of pyrazole and its biological activities. J. Pharm. Bioallied Sci. **8** (2016) 2–17.
9. Bazhin, D. N.; Kudyakova, Y. S.; Onoprienko, A. Ya.; Slepukhin, P. A.; Burgart, Y. V.; Saloutin, V. I.: Synthesis and tuberculostatic activity of functionalized pyrazoles derived from (trifluoromethyl)pyrazole containing a hydrazone group. Chem. Heterocycl. Compd. **53** (2017) 1324–1329.
10. Bruno, O.; Brullo, C.; Bondavalli, F.; Schenone, S.; Spisani, S.; Falzarano, M. S.; Varani, K.; Barocelli, V.; Ballabeni, V.; Giorgio, V.; Tognolini, M.: 1-Methyl and 1-(2-hydroxyalkyl)-5-(3-alkyl/cycloalkyl/phenyl/naphthylureido)-1*H*-pyrazole-4-carboxylic acid ethyl esters as potent human neutrophil chemotaxis inhibitors. Bioorg. Med. Chem. **17** (2009) 3379–3387.
11. Jaćimović, Ž. K.; Novaković, S. B.; Bogdanović, G. A.; Giester, G.; Kosović, M.; Libowitzky, E.: First crystal structures of metal complexes with a 4-nitro-pyrazole-3-carboxylic acid ligand and the third crystal form of the ligand. Acta Crystallogr. **C75** (2019) 255–264.
12. Latinoviić, N.; Novakoviić, S. B.; Bogdanoviić, G. A.; Kastratoviić, V.; Giester, G.; Jacimoviić, Ž. K.: Crystal structure of dihydrazinium 1*H*-pyrazole-3,5-dicarboxylate, $C_5H_{12}N_6O_4$. Z. Kristallogr. NCS **234** (2019) 957–958.
13. Jaćimović, Z. K.; Kosović, M.; Bogdanović, G.; Novaković, S. B.; Giester, G.; Bigović, M.: The crystal structure of ethyl 1-(4-nitrophenyl)-5-(trifluoromethyl)-1*H*-pyrazole-4-carboxylate, $C_{13}H_{10}F_3N_3O_4$. Z. Kristallogr. NCS **232** (2017) 651–653.
14. Foces-Foces, C.; Echevarría A.; Jagerovic, N.; Alkorta, I.; Elguero, J.; Langer, U.; Klein, O.; Minguet-Bonvehi, M.; Limbach, H.-H.: A solid-state NMR, X-ray diffraction, and ab initio computational study of hydrogen-bond structure and dynamics of pyrazole-4-carboxylic acid chains. J. Am. Chem. Soc. **123** (2001) 7898–7906.
15. Rashid, F. N. A. A.; Mohammat, M. F.; Arshad, S.; Shaameri, Z.; Hamzah, A. S.: Crystal structure of ethyl 3-(4-methoxyphenyl)-5-methylcarbamoyl-1*H*-pyrazole-4-carboxylate, $C_{15}H_{17}N_3O_4$. Z. Kristallogr. NCS **234** (2019) 1137–1139.